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Human Medicines Division

Three-year work plan for the Quality Drafting Group (QDG) of the Committee on Herbal Medicinal Products (HMPC)

Name of drafting group:	**Quality Drafting Group of the HMPC (QDG)**
Chairperson (interim):	Carmen Purdel
Vice chair:	vacant

Work plan period: **January 2024 – December 2026** (with a first review point after one year)

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1. Strategic goals

While herbal medicinal products (HMPs) are not particularly mentioned in the RSS 2025 and in the European medicines regulatory network (EMRN) some topics are relevant for herbal MPs with their emphasis on quality assessment and control.

1.1. *Short-term strategic goals*

- Provide support to HMPC on all Quality aspects for medicinal products containing herbal active substances and herbal preparations as defined in Directive 2001/83/EC as amended.
- Provide scientific and regulatory expertise under supervision of HMPC to particular questions on chemistry and analysis of herbal substances/preparations for medicinal use to EU network and support the understanding for control of complex natural compound mixtures and their relevance for safety and efficacy of MPs (incl. for SA, MDs etc.). Ensure a harmonised interpretation of EU guidelines related to Quality aspects.
- Sustain and extend harmonisation between MSs by establishing the harmonised framework of quality standards applicable for herbal MPs in the EU.
- Development of EU guidelines and identify/initiate new guidance topics as relevant. Consolidate learnings from new manufacturing technologies (e.g. supercritical CO_2 extracts, nanotechnology) and new analytical methods (e.g. quantitative NMR and near-IR spec.) for herbal medicines and provide support to training activities on implementation of priority guidelines.
- In collaboration with other parties in the European Regulatory Network, advance international regulators and stakeholder interactions: academia, interested parties, etc.
- Support the establishment of a core of European Herbal Experts, complementary to other ESECs.

1.2. *Long-term strategic goals*

- Ensure a harmonised standard for quality of marketed HMPs.
- Reinforce scientific and regulatory capacity and capability of the network and improve the scientific quality of assessments.
- Collaborate with European regulatory authorities, organisations and industry to promote further development of herbal quality standards including in response to EP, EC on new market trends such as cannabis-derived medicines.
- In collaboration with HMPC, enhance collaboration with academia.
- Maintain appropriate regulatory science knowledge management as a resource to assist the network. Develop training and tools to facilitate harmonisation of assessments.

2. Tactical goals: activities/projects to deliver the strategic goals

In contrast to most other groups at the EMA the main customer of QDG services and documents are – via HMPC- the NCAs and industry because fundamental and specific standards are mainly used in MRP/DCP and national procedures. To minor extent direct input into EMA procedures is required. The below guidelines activities (new guidelines/revisions) reflect the strategic goals listed above.

2.1. *Guideline activities*

(A) Activities to be finalised in 2024

Revision, QDG lead:

- **Guideline on Good Agricultural and Collection Practice (GACP) of starting materials of herbal origin**

Rationale: GL is outdated and recently got a lot of attention regarding the demarcation/overlap GMP vs. GACP to be clarified in view of different practices in MSs and manifold uncertainty about requirements, certification and dossier as well as differences to other GACP standards such as WHO. Significant attention is also due to substantial market activities for cannabis for medicinal use requiring GACP in national legislation. It needs to be updated to support applicants and NCAs and save resources for the Agency (many questions to EMA in this regard).

- **Guideline on the Declaration of herbal substances and herbal preparations in herbal medicinal products / traditional herbal medicinal products**

Rationale: New practices and experiences have already been identified for update of this guideline. The release of the draft revised guideline for public consultation is foreseen in 2024.

(B) Activities to be started in 2024

New guidelines, QDG lead:

- **Guidance on newly used manufacturing techniques regarding herbal preparations**

Rationale: The absence of guidance on this problem already, in particular the comparability of extracts, caused difficulties on national levels[1]. These issues (e.g. supercritical CO_2-extraction technology) are already part of the discussions on new Herbal monographs in 2020 and have shown a need for a harmonised view of HMPC.

- **Guidance on the classification and the role of markers of medicinal products qualitative analysis of herbal medicinal products and traditional herbal medicinal products**

Rationale: Markers are used for quantitative and qualitative analytical control purposes of herbal MPs and for the classification of herbal extracts. However, it is not always clear which constituents are characteristic and/or if the characteristic constituents are suitable to ensure the quality of MPs. In the view of the specific and complex nature, guidance is needed on the selection and use of markers.

[1] Court cases in MSs, with unsatisfactory outcomes

- **Guidance on comparability between herbal preparations**

Rationale: The absence of any guideline on the comparability of preparations, especially extracts, caused difficulties on national levels. Until now, only the regulatory Q&A (EMA/HMPC/345132/2010 - Rev.5) partially solved the issue when comparing the preparation with the one listed in the EU monograph. Better guidance is needed.

(C) Activities to be started in 2025

Revision, QDG lead:

- **Guideline on the quality of combinations of herbal medicinal products**

Rationale: About a third of all herbal authorisations and registrations are combination products. The GL is more than ten years old and requires updates, taking into account new Ph.Eur. standards and advanced experiences in the MSs.

New guidelines, QDG lead:

- **Guidance on the contamination of HMPs with polycyclic aromatic hydrocarbons (PAHs)**

Rationale: Following signals mainly from the food and environmental sector, the HMPC issued a reflection paper and organised a training together with industry to inform more about the topic. Several data were provided by industry. The form of appropriate guidance and possible testing needs for a group of substances according to specific intrinsic (e.g. Mate tea) or extrinsic risks (drying practices for herbal substances in some countries of origin) needs to be evaluated and decided.

(D) Activities to be started in 2026

New guidelines, QDG lead:

- **Guideline on the use of new analytical methods for the quality control of herbal medicinal products**

Rationale: A range of new analytical methods/technologies e.g. DNA-based technologies, Nuclear magnetic resonance spectroscopy, Chemometric approaches (including Multivariate analysis) and Principal component analysis and biosensors etc, are being developed and are sometimes already applied by some pharmaceutical companies in the quality control of herbal substances, herbal preparations and (traditional) HMPs. Guidance is needed to clarify the place of new analytical methods/technologies in the overall quality control system of herbal medicinal products.

2.2. *Training activities*

Continue training of quality assessors on a regular basis and build on the Herbal curriculum in the EU network training centre (EU-NTC) under the supervision of HMPC.

*Training planned for **2024:***

- Training on contaminants, microbiological testing and impurities (planed for Q1 2024).

*Training under discussion for **2024-2026:***

- Training on Certificates of suitability (CEP) (herbal substance/ preparation) and reference standards for herbals in the European Pharmacopoeia (in collaboration with EDQM).
- Training on combinations of herbal medicinal products.

- Training on the comparability of herbal preparations.
- Training referring to Good agricultural and collection practice (GACP) and Good manufacturing Practice (GMP).

2.3. *Communication and Stakeholder activities*

2.3.1. European level

Continue to engage effectively with industry through specific hearing with Interested Party on a regular basis (i.e. yearly) to gain external perspective on regulatory science needs. Strategic direction is aligned with Agency priorities (work plan development).

Extent the coordination with EDQM and provide input on the development and review of pharmacopoeia monographs and general chapters, methods and notices and to the EDQM certification of herbal active substances in view of MA and registration procedures for (traditional) HMPs.

2.3.2. International level

Contribute, comment on international developments and support representation of HMPC and EMA in herbal quality questions, in liaison with International affairs to WHO, mainly IRCH (International Regulatory Cooperation on Herbal medicines) or ICDRA (International Conference of Drug Regulatory Authorities).

2.4. *Multidisciplinary collaboration*

Maintain, or strengthen as relevant, the ongoing collaboration with other working parties and groups, e.g., QWP, GMDP-IWG as well as CMDh, NcWP. Continue to liaise and collaborate on quality-related matters with EDQM. Scientific input for the elaboration and revision of European Pharmacopoeia monographs, general chapters and notices, and to the EDQM certification of herbal active substances in view of MA and registration procedures for (traditional) herbal medicinal products.

Collaborate with the NcWP for activities related to the evaluation of potentially toxic components naturally occurring in the herbal drug / herbal preparation (e.g., pulegone, menthofuran, estragole).

3. Operational goals: medicinal product-specific activities

In contrast to most other groups at the EMA the main customer of QDG services and documents is - via HMPC - the NCAs and industry because fundamental and specific standards are mainly used in MRP/DCP and national procedures. To a minor extent, direct input into EMA procedures is required. Tactical and operational goals can be allocated to four main areas:

1. **Support for HMPC/ NCAs**
    - By drafting answers to questions of members or interested parties.
    - By responding to particular quality issues arising from HMPC assessments in the context of monograph development and mainly safety-relevant guidance.
    - Harmonisation between NCAs.
2. **Support for other groups within EMA**
    - By respond to specific herbal quality questions to HMPC by other groups such as SAWP, CHMP, PDCO or CVMP e.g. for MPs based on cannabinoids or other natural products for SA or regarding eligibility.
3. **Support of the wider EU regulatory network:**
    - Upon request of Commission or other EU agencies (EFSA, EMCDDA) provide herbal quality expert advice (e.g. on simplifications of variation regulation or cannabis distinction of products, substance and preparations).
    - Maintain and improve close coordination with EDQM, in particular Ph.Eur. expert groups 13A, 13B and TCM.
4. **Support for EMA internationally:**
    - The set of guidelines on the quality of herbal MPs are used/recognised globally as reference in international contacts (e.g. with FDA, SFDA, AYUSH, TGA and WHO).

3.1. *Pre-submission activities*

The QDG can provide input on quality questions for herbal and other MPs containing herbal substances, preparations or isolates (such as in combinations) in the framework of HMPC coordination with other EMA committees/working parties as required upon request:

- SAWP (e.g. SA procedures).
- CHMP, PDCO, COMP (e.g. eligibility, quality and composition issues).
- External requests by IPs and AskEMA.
- European Commission.

3.2. *Evaluation and supervision activities*

The QDG can provide input on quality questions for herbal and other MPs containing herbal substances, preparations or isolates (such as in combinations) in the framework of HMPC coordination with other EMA committees/working parties as required upon request:

- PRAC, CMDh (e.g. PhV issues, PSUSA and EURD for herbals).
- External requests by IPs and AskEMA.

- European Commission (e.g. approached by non-EU governmental bodies on specific herbal products).

4. Expertise

4.1. *Expertise required to achieve strategic, tactical and operational goals*

The QDG is composed of experts selected from the European experts list according to their specific expertise.

Specific expertise required linked to strategic goals:

- Phytochemistry.
- Quality control (incl. stability).
- Botany, taxonomy, plant physiology.
- Non-European traditional medicines (TCM, Ayurvedic and other Asian traditional medicines; African and American traditional medicines).
- GACP and plant cultivation.
- New analytical methods/ technologies (e.g. DNA-based technologies, Nuclear magnetic resonance spectroscopy) for quality control.
- New computational chemistry and statistical analytical methods for multi-compound mixtures (e.g. multivariate analysis, principal component analysis).
- Practical experience with the manufacture and quality of herbal substances (e.g. modern extraction technology).
- Regulatory Affairs (Herbal-specific legislation and requirements).

Supportive expertise:

- European traditional phytotherapy (classic) and other specific European traditional medicines.
- Assessment of other product types at the borderline with specific herbal relevance (medical devices, food supplements or semisynthetic products).
- Consumer protection and public health.
- Inspections/GMP/GLP/GCP.
- Microbiology.
- Biologicals, biotechnology, gene therapy, cell therapy, tissue engineering.